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Increased amygdala activation is related to heart rate during emotion processing in adolescent subjects

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Abstract

Emotions have been conceptualized as representations of bodily responses to a stimulus that critically involves the autonomic nervous system (ANS). An association between amygdala activation and ANS activity has been shown in adults. However, to date, no studies have demonstrated this association in adolescents. Examining the interaction between the ANS and amygdala in healthy adolescents may provide information about age-related changes in the association between amygdala activation and ANS measures. Therefore, the aim of this study was to examine the relationship between amygdala activation and heart rate in normal adolescents. Eighteen 12- to 17-year old adolescents participated. Heart rate data was collected during functional magnetic resonance imaging while subjects performed a facial expression matching task that reliably activates the amygdala. Adolescents showed significant amygdala activation for all facial expressions relative to the shape-matching, control task. Moreover, the degree of activation in the right amygdala for Fearful faces was significantly correlated with heart rate (Spearman's rho = 0.55, $p = 0.018$, two-tailed). This study shows that amygdala activity is related to heart rate in healthy adolescents. Thus, similar to adults, adolescents show a coupling between processing emotional events and adjusting the ANS accordingly. Furthermore, this study confirms previous adolescent studies showing amygdala activation to Fearful, Angry, and Happy faces. Finally, the results of the present study lay the foundation for future research to investigate whether adolescents with mood or anxiety disorders show an altered coupling between processing emotionally salient events and ANS activity.

Keywords: Amygdala; Adolescent; Emotions; fMRI; Heart Rate; Autonomic Nervous System

The James-Lange theory of emotion posits that an emotion is a perceived central representation of bodily responses to a stimulus [13,17]. As part of this theory, emotional feelings are dependent on physiological bodily responses that are generated automatically by the autonomic nervous system (ANS). The amygdala is an important part of the limbic system that is well positioned to control basic autonomic arousal processes. Through the hypothalamus and brainstem circuits, the amygdala innervates the autonomic networks and produces visceral signs of emotional arousal—e.g., changes in heart rate [18].

Neuroimaging studies suggest that examination of the amygdala may be of particular significance in psychiatric illnesses. Functional MRI studies in adults have shown abnormal amygdala activity in depression [31], schizophrenia [29], bipolar disorder [40], post-traumatic stress disorder [32], and autism [26]. In pediatric populations, fMRI studies have demonstrated abnormal amygdala activity in depression [35], anxiety disorders [35], bipolar disorder [27], autism [8], and conduct disorder [33]. Furthermore, structural MRI studies of the amygdala have found abnormalities in patients with depression [28], dissociative identity disorder [36], and autism [14].

The amygdala appears to play an especially important role in normal and abnormal adolescent behavior. In the triadic model of adolescent development, the authors propose that perturbations in the neural development of the components of this system (e.g., amygdala) may contribute to the expression of adoles-

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cent psychopathology [5]. For example, the authors suggest that abnormal maturation of the amygdala during adolescence may lead to greater vulnerability to psychiatric disorders such as depression and anxiety. The authors cite both functional [35] and structural [28] MRI studies of the amygdala in pediatric depression and anxiety to support their theory.

Given the amygdala's influence on the ANS and its role in emotion, a logical step would be to pursue the simultaneous recording of physiological and functional neuroimaging data. To examine concomitant changes in emotional arousal, skin conductance was recorded with fMRI in a study of the amygdala's response to facial signals of fear in normal adults [37]. The researchers observed that mean skin conductance level was positively correlated with right amygdala activity. By using different pressor challenges to elevate blood pressure, two fMRI studies in normal adults found that the pressor challenges elicited significant regional fMRI signal changes in the amygdala [11,12]. To address the question of central control of heart rate in emotions, parallel measurement of heart rate changes and changes in activation as indexed by fMRI was performed on normal adults [15]. This study found that the amygdala was an integral part of the central circuit controlling heart rate in negative affect (e.g., fear).

Although rare, two published human depth electrode studies exist that are pertinent. In two similar studies, the authors recorded electrocardiogram activity together with single cell activity from the amygdala in epileptic patients undergoing chronic depth electrode monitoring [6,7]. The authors discovered that changes in heart rate correlated with the firing of neurons in the human amygdala.

Other fMRI studies in normal adults have found additional brain regions that are activated in association with the ANS. In one study where brain activity and heart rate were simultaneously measured, the authors found that the level of activity in the amygdala, insula, anterior cingulate, and brainstem predicted subjects' heart rate responses to the presentation of emotional facial expressions [4]. By examining neural activity related to modulation of skin conductance level, another fMRI study reported that activity within the insular cortices, anterior cingulate, striate and extrastriate cortices, thalamus, and hypothalamus reflected the rate of change in electrodermal activity [23]. Although studies combining fMRI and physiological measurements have been done in adults, to our knowledge, no such studies have been published in the pediatric population.

The purpose of this study was to use blood oxygenation level dependent fMRI (BOLD-fMRI) in combination with the simultaneous acquisition of physiological data to examine the relationship between amygdala activation and heart rate in normal adolescents. To this end, we used an emotional face paradigm that has been shown in fMRI studies to robustly activate the amygdala [25] and well-established methods of heart rate data analysis [9,34]. We hypothesized that the adolescent amygdala would be activated in response to the perception of Fearful, Angry, and Happy faces relative to the control condition. Furthermore, based upon the human depth electrode studies [6,7] and fMRI findings [4], we hypothesized that an increased amygdala fMRI BOLD signal due to the perception of Fearful, Angry, and Happy faces compared to the control condition would be correlated with an increased heart rate in adolescent subjects.

This study was approved by the University of California at San Diego (UCSD)-Children's Hospital and Health Center (CHHC) Institutional Review Board and conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki). All subjects provided written assent, and their parent/legal guardians provided written informed consent to participate.

Eighteen healthy, right-handed adolescent subjects (15 females and 3 males; ages 13–17 years; mean age 16.17 ± 1.20 years) were recruited from all regions of San Diego.

Each participant was administered: (1) Computerized Diagnostic Interview Schedule for Children version 4.0 [30] and the Diagnostic Predictive Scale (DPS) [19] to assess for the presence of any Axis I diagnoses, (2) Standard Snellen Eye Chart, (3) Ishihara Color Plates Test (8 plate, 2005 edition), and (4) Edinburgh Handedness Inventory [24]. Furthermore, each participant completed the following self-administered questionnaires: (1) demographics questionnaire and (2) medical and developmental history form. Exclusion criteria for this study were: (1) any current or lifetime DSM-IV Axis I psychiatric disorder, (2) color blindness, (3) less than 20/40 corrected vision, (4) history of a serious medical, developmental, or neurological disorder, (5) history of loss of consciousness greater than 2 minutes, (6) left handedness, (7) MRI contraindications (ferrometallic implants, braces, pregnancy or claustrophobia), and (8) inability to fully comprehend and cooperate with study procedures.

All participants were trained to perform the emotional face task prior to fMRI scanning. During the scan, each participant was shown a modified [25] version of the task by Hariri et al. [10]. For each trial, a target face was presented at the top of the screen and two probe faces were presented at the bottom. The participants were asked to match the target face with one of the two probe faces that had the same emotional expression by pressing the left or right button on a Current Designs box. Each block contained six consecutive, 5-s trials where the target was a Fearful, Happy, or Angry face. The control task consisted of 5-s trials of either tall or wide circles or ovals in a similar configuration to the facial expression task. Analogous to the facial expression task, participants were told to match the shape of the target to one of the two probes in the control task. There were a total of 12 blocks: 3 blocks for each of the Fearful, Happy, and Angry faces, and 3 blocks of the control task. Blocks were separated by a 10-s fixation cross and a 2-s instruction period. In addition, a brief fixation was added to the start and end of the task to make a total task time of 512 s.

Images were acquired on a 3-T GE scanner (General Electric, Milwaukee, WI) with Twin Speed gradients using a GE 8-channel head coil. Each session consisted of a three-plane scout scan (10 s), a high-resolution anatomical scan, a series of T2*-weighted echo-planar imaging (EPI) scans to measure the blood oxygen-level dependent (BOLD) response, and EPI-based field maps to correct for susceptibility induced geometric distortions. Functional scans covering the entire